REMARKS

On page 2 of the Office Action (Paper No. 20080418), the Examiner issued a four-way restriction requirement pursuant to 35 USC §§ 121 and 372. The restriction divided the claims into the following allegedly distinct inventions: Group I containing claims 1-5, drawn to polynucleotide comprising SEQ ID NO: 1 encoding enone reductase enzyme, vector and transformant expressing said polynucleotide; Group II containing claim 6, drawn to enone reductase polypeptide encoded by polynucleotide of SEQ ID NO: 1; Group III, containing claim 7, drawn to production of levodione using enone reductase polypeptide encoded by polynucleotide of SEQ ID NO: 1; and Group IV, containing claim 8, drawn to production of levodione using transformed host cell expressing polynucleotide comprising SEQ ID NO: 1. (*Id.*)

Initially, we observe that the Examiner has mischaracterized the scope of the claims. In the restriction requirement, "SED ID NO: 1" is repeatedly referenced, but SEQ ID NO: 1 is only recited in claim 3. Thus, to the extent the Examiner interpreted, *e.g.*, claims 1-2 and 4-8 as limited to SEQ ID NO: 1, the restriction requirement is based on an erroneous understanding of the claims and must be withdrawn for this reason alone.

In issuing the restriction requirement, the Examiner asserted that the inventions "do not relate to a single general inventive concept under PCT Rule 13.1 because...they lack the same or corresponding special technical features..." (*Id.*).

In accordance with restriction practice, the subject matter of claim 7 (Group III) is hereby elected for prosecution with traverse.

Notwithstanding the foregoing election, we respectfully traverse the restriction for the reasons below.

In making the restriction requirement, the Examiner acknowledged that "[g]roups II-III pair share a technical feature" and that "[g]roups I & IV pair share a technical feature." (Id. at 3.) The Examiner, however, asserted that "[the] shared technical feature [l]inking group[s] I-IV, enone reductase, does not constitute a 'special technical feature' as defined by PCT Rule 13.2, because it does not claim a feature which defines a contribution over the prior art as enone reductase of claim 1 is taught by Wanner et al. (E.J. Biochem. 1998, 255 pp 271-278...)." (Id.)

The document cited by the Examiner, Wanner *et al.* (E.J. Biochem. 1998, 255 pp 271-278) ("Wanner") discloses "[t]wo enone reductases catalyzing irreversibly the enantiomeric reduction of α,β-unsaturated carbonyls [which] have been purified [from] *Saccharomyces cerivisiae* ...". (Abstract, lines 1-3.) Wanner also discloses that "[o]ne enzyme (E I) was NADPH-dependent, showed a molecular mass of 75 kDa and decomposed under denaturing electrophoretic conditions into two subunits of 34 kDa and 37 kDa. The other enzyme (E II) was NADH linked and the [estimated] molecular mass ... was 130 kDa. The enzyme decomposed into subunits of 56 kDa and 64 kDa on SDS/PAGE." (Abstract, lines 5-8.) Wanner further discloses that "[b]oth enzymes were most active at pH 4.8 ...". (Abstract, line 9.)

The restriction requirement cannot stand because Wanner does not disclose the enone reductase of the claims, and as such, the shared technical feature linking groups I-IV constitutes a special technical feature under PCT Rule 13.2. (As noted above, the Examiner identified the enone reductase as the "shared technical

feature [l]inking group[s] I-IV". (Paper No. 20080418 at 3.)) Wanner discloses two enone reductases from the yeast *Saccharomyces cerevisiae*, each of which differs from the enzyme recited in the claims. The first Wanner enzyme (E I) shows a molecular mass of ***75 kDa***. (Abstract, line 5; Page 274, column 2, line 2, reciting 76 kDa.) Upon electrophoretic separation on SDS/PAGE under denaturing conditions, E I "decompose[s] into two subunits of 34 kDa and 37 kDa". (Page 274, column 2, lines 5-6; Abstract, lines 5-6.) The second Wanner enzyme (E II) shows a molecular mass of ***130 kDa*** (Abstract, lines 7-8: Page 274, column 2, lines 1-2), and it "decompose[s] into subunits of 56 kDa and 64 kDa" under the same conditions on SDS/PAGE. (Page 274, column 2, lines 6-7; Abstract, lines 7-8.) Wanner, which discloses enzymes E I and E II having a molecular mass of 75 kDa and 130 kDa, respectively, does not disclose the "enzyme having enone reductase activity wherein the enzyme is characterized by ... (a) molecular mass of 61,300±5,000 Da ..." (i.e., 56.3 to 66.3 kDa) as recited in, *e.g.*, claim 1.

Also, Wanner discloses that "[b]oth enzymes had identical pH optima at 4.8. The temperature optima of the enzymes have been found between 30-38°C (Fig. 5)." (Page 275, column 1 under heading "Effects of pH and Temperature.") The enzyme recited in claim 1, on the other hand, "is characterized by the following physico-chemical properties : . . . (d) optimum temperature: 55-60°C at pH 7.4; and (e) optimum pH: pH 4.5-8.5." Thus, the optimum temperature of the Wanner enzymes differs from that recited in, *e.g.*, claim 1.

And, as noted above, Wanner discloses that its "enzyme (E I) was NADPH-dependent," and its enzyme (E II) was NADH linked." (Abstract, lines 5 and 7.)

Wanner further discloses that E I and E II separated upon column chromatography of the enzyme extract as "two activities with different coenzyme dependency (Fig. 1). At about 0.2M NaCl the main activity required NADPH (E I) as coenzyme; at about 0.43 M NaCl a second activity requiring NADH (E II) was found. Residual activity with the alternative coenzyme was lost in each case after . . . affinity chromatography and resulted in an ***exclusive dependency of NADPH for E I and NADH for E II.***" (Page 273, column 2, 4th to last line to page 274, column 1, line 6) (emphasis added.) Wanner discloses in addition that although "E II possessed a similar substitute specificity as E I[,] ***[t]he coenzymes could not be replaced by each other***. . .". (Page 277, column 1, lines 22-24) (emphasis added.)

Wanner, which discloses "exclusive dependency" of cofactors NADPH and NADH for its E I and E II enzymes, does not disclose "an enzyme having enone reductase activity wherein the enzyme is characterized by ... (b) co-factor: NADPH and NADH" as recited in claim 1. As disclosed in the present application:

> The enone reductase of the present invention catalyzes the reduction of ketoisophorone to levodione in the presence of a co-factor, NADH or NADPH, according to the following formula:
>
> Ketoisophorone + NADH (NADPH) $\rightleftharpoons$ Levodione + NAD (NADP)
>
> (Specification, Page 6, lines 1-4.)

For each of the foregoing reasons, it is submitted that the Examiner has erred in asserting that the enzyme "of claim 1 is taught by [Wanner]". (Paper No. 20080418 at 3.) Thus, the alleged "shared technical feature [l]inking group[s] I-IV, enone reductase", as referred to by the Examiner, does constitute a "special technical

feature as defined by PCT Rule 13.2...". (Id.) Accordingly, the unity of invention requirement is fulfilled. For this reason, reconsideration and withdrawal of the requirement for restriction is respectfully requested.

Early and favorable action is respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned attorney.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Mail Stop Amendment, Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on June 19, 2008.

Eileen M. Ebel, Reg. No. 37,316

Respectfully submitted,

By: _____

Eileen M. Ebel
Registration No. 37,316
BRYAN CAVE LLP
1290 Avenue of the Americas
New York, NY 10104-3300
Phone: (212) 541-2000
Fax: (212) 541-4630